

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/040438

International filing date (day/month/year)
03.12.2004

Priority date (day/month/year)
03.12.2003

International Patent Classification (IPC) or both national classification and IPC
C12N9/16, C12N9/50, C12N9/52

Applicant
GENENCOR INTERNATIONAL, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/US2004/040438

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/040438

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. Invention 1: claim 4, 119 and 120 completely, and claim 1-3,5-7,68,70-84,86,87,118,121-125,127-135,153-158,and 163-166 partially

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-7,68,70-84,86,87,118-125,127-135,153-158,163-166
	No: Claims	
Inventive step (IS)	Yes: Claims	1-7,68,70-84,86,87,118-125,127-135,153-158,163-166
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-7,68,70-84,86,87,118-125,127-135,153-158,163-166
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)
and / or
2. Non-written disclosures (Rules 43*bis*.1 and 70.9)
see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

PCT/US2004/040438

1. The following documents (D) cited in the search report, are referred to in this communication; their numbering will be adhered to during the rest of the procedure:

- D1: US-A-5 352 594 (POULOUSE ET AL) 4 October 1994 (1994-10-04)
- D2: EP-A-0 375 102 (THE CLOROX COMPANY) 27 June 1990 (1990-06-27)
- D3: DATABASE UniProt [Online] 1 December 2001 (2001-12-01), "Hypothetical protein." XP002330234 retrieved from EBI accession no. UNIPROT:Q92XZ6 Database accession no. Q92XZ6
- D4: DATABASE UniProt [Online] 1 October 2001 (2001-10-01), "Arylesterase." XP002330235 retrieved from EBI accession no. UNIPROT:Q98MY5 Database accession no. Q98MY5
- D5: DATABASE UniProt [Online] 1 June 2003 (2003-06-01), "Lipase, GDSL family." XP002330247 retrieved from EBI accession no. UNIPROT:Q88KH2 Database accession no. Q88KH2
- D6: WO 2004/058961 A (HENKEL KOMMANDITGESELLSCHAFT AUF AKTIEN; WIELAND, SUSANNE; POLANYI-BAL) 15 July 2004 (2004-07-15)

2. The application provides a perhydrolase obtained from *Mycobacterium smegmatis* with a higher perhydrolase activity than a hydrolase activity. Perhydrolases with a perhydrolase to hydrolase activity ratio of up to 1 are known from the prior art; see e.g. D1 and D2. A ratio of larger than 1 appears to be new.

3. The perhydrolase represented by SEQ.ID.2 and encoded by SEQ.ID.1 appears to be quite unrelated in primary structure to previously known hydrolases, proteases, lipases, or any other enzyme with putative perhydrolase activity. In view of its unexpected and desirable properties, it must also be regarded as inventive in the sense of Art.33(3) PCT and industrially applicable in accordance with Art.33(4) PCT.

4. The present claims are however largely directed to structural (other than primary structure) homologues of the protein actually disclosed and mutants thereof. The applicant argues in the description that since enzymes with comparable activities are structurally related, but have very divergent amino acid sequences, this would appear to represent a fair generalization of the invention.

It is however not clear in the sense of Art.6 PCT what is encompassed in the scope of such claims. Furthermore, there is no indication that any or all of these structurally enzymes have the advantages ratio between perhydrolase and hydrolase activities. If the teaching of the application is that all structurally related enzymes comprising the motifs identified in claim 73 possess this property, then such enzymes and the claims covering them are not new in the sense of Art.33(2) PCT, since such enzymes are disclosed in e.g. D3-D5, proteins which by the way have respectively about 65, 40 and 30% sequence identity with SEQ.ID.2.

If that is not the teaching of the application, then the application does not show how the skilled person is supposed to arrive at the subject-matter of the invention without undue burden or the application of inventive skill, in which case the same claims are objectionable under Art.5 PCT for lack of enabling disclosure.

The ISA considers that mutants of SEQ.ID.2 can be considered as a fair generalization of the teaching of the invention to the extent that it can reasonably be expected that they keep the advantageous properties of the mother protein. Since the present claims do not limit the total number of mutated residues, and the number of proposed mutations in total covers all but 29 of the 216 residues, the ISA considers the scope of the present claims, even to the extent that they would be limited to mutants of the protein of SEQ.ID.2, as too broad to be considered as supported in the sense of Art.6 PCT, nor are all of those mutants disclosed in accordance with Art.5 PCT.

5. This ratio between the perhydrolase and hydrolase activities appears to be pH-dependent, although the claim does not specify the conditions under which it is measured, leading to a lack of clarity under Art.6 PCT.